

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

DEC 19

## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

To:  
CATHY KODROFF  
HOWSON AND HOWSON  
SRPING HOUSE CORPORATE CENTER  
P.O. BOX 457  
SPRINGS HOUSE, PA 19477

Date of mailing (day/month/year)	16 DEC 2005
Applicant's or agent's file reference UPN-Q3355PCT	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. PCT/US05/01768	International filing date (day/month/year) 21 January 2005 (21.01.2005)
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.  

**Filing of amendments and statement under Article 19:**  
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
  - ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Reminders**  

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide, Volume II, National Chapters and the WIPO Internet site.

5/11/06 (Art 1)  
3/16/06 Demand

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Suzanne M. Mayer, Ph.D. Telephone No. 571-272-1600
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UPN-Q3355PCT	<b>FOR FURTHER ACTION</b> <div style="font-size: small; margin-top: 5px;">             see Form PCT/ISA/220              as well as, where applicable, item 5 below.           </div>	
International application No. PCT/US05/01768	International filing date ( <i>day/month/year</i> ) 21 January 2005 (21.01.2005)	(Earliest) Priority Date ( <i>day/month/year</i> ) 23 January 2004 (23.01.2004)
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the language, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box No. II)

3. ☐ Unity of invention is lacking (See Box No. III)

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_

- ☐ as suggested by the applicant.
- ☐ as selected by this Authority, because the applicant failed to suggest a figure.
- ☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

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PCT/US05/01768

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

# INTERNATIONAL SEARCH REPORT

PCT/US05/01768

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 9-15  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Claims 9-15 were unsearchable as they are dependent upon any of claims 1-8; where there is no claim 3.
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

PCT/US05/01768

A. CLASSIFICATION OF SUBJECT MATTER																						
IPC(7) : C07K 1/00, 14/00; C07H 21/02, 21/04; A61K 31/70																						
US CL : 530/350, 827; 536/23.1-23.5; 514/44																						
According to International Patent Classification (IPC) or to both national classification and IPC																						
B. FIELDS SEARCHED																						
Minimum documentation searched (classification system followed by classification symbols) U.S. : 530/350, 827; 536/23.1-23.5; 514/44																						
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched																						
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) BioSci, Medicine, Caplus, Medline (in Dialog), PTO internal, Sequence databases-PTO internal and NPL: utrophin, dystrophin-related protein, dystrophin-like protein, DLP, DRP.																						
C. DOCUMENTS CONSIDERED TO BE RELEVANT																						
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																				
X	US 6,518,413 B1 (TINSLEY et al.) 11 February 2003 (11.02.2003), Examples 1-2, column 12-17.	1,2,4,5,7-8 and 16-17																				
A	WO 01/25461 A1 (BURTON et al.) 12 April 2001 (12.04.2001), Abstract and claims 1-10.	7-8																				
A	GILBERT et al., Improved Performance of a Fully Guttet Adenovirus Vector Containing Two Full-Length Dystrophin cDNAs Regulated by a Strong Promoter. Molecular Therapy. October 2002. Vol. 6, No. 4, pp. 501-509. p. 502, 2nd column, 1st paragraph; pp. 502-503 and p. 507, 1st column, last two paragraphs.	1,2,4,5,7,8,16 and 17																				
L	VAN DEUTEKOM et al., Advances in Duchenne Muscular Dystrophy Gene Therapy. Nature Reviews Genetics. October 2003. Vol. 4, pp. 774-783. Figure 1. Shows Utrophin only has two hinge regions.	2																				
L	WINDER et al. Dystrophin and Utrophin: The Missing Link. FEBS Letters. 1995. Vol. 369, pp. 27-33. See p. 28, 1st column, 1st line.	2																				
A	BARANOV et al. The Current State and Prospects of the Gene Therapy of Duchenne Muscular Dystrophy Worldwide and in Russia. Russian Journal of Genetics. 2001. Col. 37, No. 8, pp. 868-875. Entire Document.	1,2, 4-8 and 16-17																				
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																						
* Special categories of cited documents: <table border="0"> <tr> <td>"A"</td> <td>document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T"</td> <td>later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E"</td> <td>earlier application or patent published on or after the international filing date</td> <td>"X"</td> <td>document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L"</td> <td>document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y"</td> <td>document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O"</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"P"</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>			"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family	"P"	document published prior to the international filing date but later than the priority date claimed		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention																			
"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone																			
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art																			
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family																			
"P"	document published prior to the international filing date but later than the priority date claimed																					
Date of the actual completion of the international search 07 November 2005 (07.11.2005)		Date of mailing of the international search report 16 DEC 2005																				
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Suzanne M. Mayer, Ph.D. Telephone No. 571-272-1600																				

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/01768

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TINSLEY et al. Primary Structure of Dystrophin-Related Protein. Nature. December 1992. Vol. 360, pp.591-593. Entire Document.	1,2, 4-8 and 16-17
A	PERKINS et al. The Role Utrophin in the Potential Therapy of Duchenne Muscular Dystrophy. Neuromuscular Disorders. 2002. Vol. 12, pp. S78-S89. Entire Document.	1,2, 4-8 and 16-17
A	WILSON et al. Up71 and Up140, Two Novel Transcripts of Utrophin That Are Homologues of Short Forms of Dystrophin. Human Molecular Genetics. 1999. Vol. 8, No. 7, pp. 1271-1278. Entire document.	1,2, 4-8 and 16-17
A	AMANN et al. Utrophin Lacks the Rod Domain Actin Binding Domain of Dystrophin. The Journal of Biological Chemistry. December 1999. Vol. 274, No. 50, pp. 35375-35380. Entire Document.	1,2, 4-8 and 16-17
A	ATHENA et al., Cloning and Expression of Full Length Mouse Utrophin: The Differential Association of Utrophin and Dystrophin with AChR Clusters. FEBS Letters. 1996. Vol. 398, pp. 259-264. Entire Document.	1,2, 4-8 and 16-17
A	SQUIRE et al. Prevention of Pathology in mdx Mice by Expression of Utrophin: Analysis Using an Inducible Transgenic Expression System. Human Molecular Genetics. 2002. Vol. 11, No. 26, pp. 3333-3344. Entire Document.	1,2, 4-8 and 16-17

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
CATHY KODROFF  
HOWSON AND HOWSON  
SRPING HOUSE CORPORATE CENTER  
P.O. BOX 457  
SPRINGS HOUSE, PA 19477

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing (day/month/year) <b>16 DEC 2005</b>	
Applicant's or agent's file reference <b>UPN-Q3355PCT</b>	
<b>FOR FURTHER ACTION</b> See paragraph 2 below	
International application No. <b>PCT/US05/01768</b>	International filing date (day/month/year) <b>21 January 2005 (21.01.2005)</b>
Priority date (day/month/year) <b>23 January 2004 (23.01.2004)</b>	
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): C07K 1/00, 14/00; C07H 21/02, 21/04; A61K 31/70 and US Cl.: 530/350, 827; 523.1-23.5; 514/44</b>	
Applicant <b>THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA</b>	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☒ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☒ Box No. VII      Certain defects in the international application
- ☒ Box No. VIII      Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion <b>07 November 2005 (07.11.2005)</b>	Authorized officer <b>Suzanne M. Mayer, Ph.D.</b> Telephone No. 571-272-1600
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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/01768

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☒ on paper  
☒ in electronic form

c. time of filing/furnishing

- ☒ contained in the international application as filed.  
☒ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International appl  
PCT/US05/01768

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application  
☒ claims Nos. 9-15

because:

- ☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international search (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 9-15 are so unclear that no meaningful opinion could be formed (*specify*):

The claims are dependent upon 'any of claims 1-8'. There is no claim 3 in the application thus no meaningful search of these claims can be made.

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

- ☐ no international search report has been established for said claims Nos. \_\_\_\_\_

- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International appl.  
PCT/US05/01758  
1

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>6</u>	YES
	Claims <u>1,2,4,5,7-8 and 15-16</u>	NO
Inventive step (IS)	Claims <u>6</u>	YES
	Claims <u>1,2,4,5,7-8 and 15-16</u>	NO
Industrial applicability (IA)	Claims <u>1,2,4-8 and 15-16</u>	YES
	Claims <u>1,2,4-8 and 15-16</u>	NO

**2. Citations and explanations:**

Claims 1,2,4,5, 7-8 and 16-17 lack novelty and inventive step under PCT Article 33(2) and 33(3) as being anticipated by TINSLEY et al. (US 6,518,413). Utrophin is a 3,433 amino acid protein with several different regions and domains and which is usually found in muscle tissues. Tinsley et al. teach a DNA molecule that is a utrophin "mini-gene" which expresses a polypeptide that encodes for a 2008 amino acid protein which possesses the N-terminal amino acid domain, and the C-terminal amino acid domain, but which is missing the majority of the central domain (approximately 1500 amino acids - attached amino acid sequence alignment of SEQ ID No: 5 and SEQ ID No: 8 of Tinsley et al.). The polynucleotide is clone is placed under the control of the human skeletal alpha-actin (HAS) promoter and regulatory regions (column 16, lines 55-62). This promoter is a muscle specific promoter. The DNA of the invention is used with adenovirus or retrovirus vectors (column 10, lines 1-3). Claim 2 is included in this rejection because the prior art suggests/teaches that utrophin only has two hinge regions. This is evidenced by van Deutekom et al. (Figure 1, p.776) and Winder et al.: "similarly utrophin is thought to contain 22 repeats and two hinges." (1<sup>st</sup> column, 1<sup>st</sup> line, p.28).

Claim 6 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest DNA that encodes a protein of SEQ ID Nos: 4, 2 and 5.

Claims 1-2, 4-8 and 16-17 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. The microtrophin DNA and encoded proteins described in this application would be useful in the medical industry as a potential treatment supplement for muscle wasting diseases such as muscular dystrophy.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/01768

**Box No. VII Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: The first page of the specification is missing.

The Brief Description of the Drawings section contains an error on p. 2, line 19. This line refers to Figures 3A-2K, it should refer to Figures 3A-3K.

Claims 1-17 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: There is no claim # 3 in the claim set. Thus the claims are incorrectly numbered after claim 2 and onwards.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/01768

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 2-8 and 16-17 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 2-8 and 16-17 are indefinite for the following reason(s): The independent claim is drawn to a DNA molecule. However, the inconsistent use of DNA terminology and protein (e.g. amino acid) terminology renders the claims indefinite. For example, in claim 6, the recitation of a nucleic acid according to claim 1, where the microtrophin is selected from the group having the amino acid sequence of SEQ ID No: 4. Correct claim construction in this circumstance dictates that the nucleic acid must encode for a protein having an amino acid sequence.

Claim 6 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 6 is indefinite for the following reason(s): Claim 6 recites a microtrophin selected from the group consisting of human, canine and mouse microtrophin having the amino acid sequences of SEQ ID Nos: 4, 2 and 5, respectively. However, "microtrophin" is not a naturally occurring protein. Instead the term is defined by Applicants themselves and it they are non-naturally occurring protein derived from human, canine and mouse, but not endogenous. Thus, claims a human microtrophin having the amino acid sequence of SEQ ID No: 4, for example, is wholly inaccurate and misleading.

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